SH@W Safety and Health at Work www.e-shaw.org

Saf Health Work 2012;3:58-66 | http://dx.doi.org/10.5491/SHAW.2012.3.1.58

pISSN : 2093-7911
eISSN : 2093-7997

Original Article

Outbreak of Sudden Cardiac Deaths in a Tire Manufacturing Facility: Can It Be Caused by Nanoparticles?

Eun-A KIM[1], Jungsun PARK[1], Kun-Hyung KIM[1], Naroo LEE[1], Dae-Seong KIM[1] and Seong-Kyu KANG[2]

[1]Occupational Safety and Health Research Institute
[2]Korea Occupational Safety and Health Agency, Incheon, Korea

Objectives: The purpose of this study was to review clinical characteristics and working environments of sudden cardiac death (SCD) cases associated with a tire manufacturer in Korea, and review possible occupational risk factors for cardiovascular disease including nanoparticles (ultrafine particles, UFPs).
Methods: We reviewed (i) the clinical course of SCD cases and (ii) occupational and non-occupational risk factors including chemicals, the physical work environment, and job characteristics.
Results: Possible occupational factors were chemicals, UFPs of rubber fume, a hot environment, shift work, overworking, and noise exposure. The mean diameter of rubber fume (63-73 nm) was (larger than diesel exhaust [12 nm] and outdoor dust [50 nm]). The concentration of carbon disulfide, carbon monoxide and styrene were lower than the limit of detection. Five SCD cases were exposed to shift work and overworking. Most of the cases had several non-occupational factors such as hypertension, overweight and smoking.
Conclusion: The diameter of rubber fume was larger than outdoor and the diesel exhaust, the most well known particulate having a causal relationship with cardiovascular disease. The possibility of a causal relation between UFPs of rubber fume and SCD was not supported in this study. However, it is necessary to continue studying the relationship between large sized UFPs and SCD.

Key Words: Cardiac arrest, Rubber, Nanoparticles, Heat stress disorder, Shift work

Introduction

From May 2006 to September 2007, 7 cases of sudden cardiac death (SCD) were reported from a tire manufacturing factory in Korea [1]. Five of them were found to have ischemic heart disease (IHD; I20-I25 of the International Statistical Classification of Diseases and Related Health Problems [ICD] 10th Revision) at autopsy. The other two, who could not undergo autopsy, were suspected to have had cardiac arrest due to unknown causes. Several non-governmental organizations suspected that various chemicals or nanoparticles might be the cause of the outbreak. The Occupational Safety and Health Research Institute of the Korea Occupational Safety and Health Agency conducted an epidemiologic investigation from October 2007 to February 2008, to find possible causal risk factors.

Although many adverse health effects including carcinogenic [2], respiratory [3], dermatologic [4,5], reproductive [6], and musculoskeletal [7,8] effects or injuries have been reported to be related with rubber tire manufacturing, only a few studies

Received: November 7, 2011, **Revised:** December 8, 2011
Accepted: December 8, 2011, **Available online:** March 8, 2012
Correspondence to: Jungsun PARK
Occupational Safety and Health Research Institute
Korea Occupational Safety and Health Agency
478, Munemi-ro, Bupyeong-gu, Incheon 430-711, Korea
Tel: +82-32-510-0710, **Fax:** +82-32-518-6486
E-mail: jsunpark@chol.com

have dealt with cardiovascular diseases (CVD) and tire manufacturing [9-12]. Since most cases of sudden cardiac arrest are supposed to have underlying IHD, including coronary heart disease (CHD) [13], the occupational and non-occupational risk factors for CHD and the triggering factors of SCD were reviewed.

Several chemicals-carbon disulfide [9], nitrites [14], methylene chloride [15], carbon monoxide [16]), physical factors (noise [17]), and working conditions (job stress [18], long working hours, and shift work [19,20]- are on the list of well known occupational risks related to CHD. High [21] or low [22] temperature, and chlorofluorocarbons [23,24] are also reported as factors that trigger SCD from CHD. A nanoparticle is defined as a particulate having an aerodynamic diameter ≤ 0.1 μm, which is also called an ultrafine particle (UFP). Epidemiological studies in the past have provided strong evidence that elevated levels of ambient fine particulates (aerodynamic diameter ≤ 2.5 μm [particulate matter, PM 2.5]) or UFPs are associated with increased cardiovascular morbidity or mortality with exacerbations of ischemic and/or arrhythmic cardiac diseases [25,26]. Available clinical and experimental evidence supports several mechanisms mediating the cardiovascular effects of particles, such as inflammatory responses [27], dysfunction of the autonomic nervous system [27], and cardiac malfunction [28]. However, the relationship between PM and cardiac disease is not fully understood [29]. Because the characteristics of rubber fume, the major portion of the particulates in rubber tire manufacturing, had never been reported, we had no information regarding the correspondence of rubber fume to UFP.

Therefore, the purpose of this study was to describe the detailed clinical course and working environment of the SCD cases from a tire manufacturer in Korea, and review possible relationships between chemical and physical factors including PM or UFPs and SCDs.

Materials and Methods

The clinical course, working environment, and specific duties of the seven SCD cases were reviewed. In December 2007, several chemical (carbon disulfide, styrene, rubber fume, and

Table 1. Clinical course of the seven sudden cardiac death (SCD) cases

Plant	Case No.	Age at arrest	Date of death, time (season)	Autopsy (ICD10 code)	Location of death	Behavior of the cases during 24 hours before death
A	1	44	September 07, 05:00 (autumn)	SDC (I46.1)*	Found by coworkers as fallen on bathroom of his home	Working for morning shift and rest or sleeping at home
A	2	35	April 07, 12:50 (spring)	DCMP (I42)	Found convulsive state during sleeping by his family at home	Working for night shift, having breakfast with alcohol drinking, and sleeping
A	3	51	May 06, 12:00 (spring)	SDC (I46.1)*	Fainting during resting at home	Working for afternoon shift, visiting parent's house in the next morning to help the transplanting of rice plants in the field, and took a nap
B	4	49	July 06, 08:00 (summer)	IHD (I25)	Found as unconscious at dressing room of the company	Working for night shift from last 22:00 to 06:00 and moved to day shift and started his duty from 8:00 to 14:00 at the same day, resting until next morning and went to work
B	5	41	November 06, 18:00 (winter)	IHD (I20~25)	Fainting at a restaurant before having dinner with friend	Working for morning shift, watching soccer game with drinking, and go to restaurant for dinner
C	6	27	December 06, 05:00 (winter)	AMI (I21)	Found by coworkers at dormitory apartment	Working until 18:00 and had department dinner for 2 hours and sleeping at dormitory apartment
C	7	29	May 07, 05:00 (spring)	AMI (I21)	Found by coworkers at dormitory apartment	Because of weekend off, resting and sleeping

ICD10: International Classification of Disease 10th Revision, NA: not available, DCMP: dilated cardiomyopathy, IHD: ischemic heart disease, AMI: acute myocardial infarction.
*Clinical diagnosis due to lack of autopsy result.

carbon monoxide) and physical (noise and high temperature) risk or triggering factors of ICD or SCD, were assessed. In addition, several chemicals with an unclear relationship to CVD were analyzed. They were cyclopentane, hexane, n-hexane, cyclohexane, heptanes, methylcyclohexane, formaldelyde, sulfur dioxide, and methylisobutylketone. The detailed results of these environmental measurements were described in the final report of the epidemiological investigation [1]. In October 2008, we conducted an assessment of the rubber fume PM at the nano-scale, at the curing and calendering process [30]. PM was measured around a diesel-powered forklift to evaluate diesel exhaust, one of the most well-studied UFPs, and outdoors, to evaluate background levels of UFPs. The mean diameter and surface of the rubber particles were measured by a Scanning Mobility Particle Sizer Spectrometer (GRIMM #5.403; GRIMM Inc., Douglas Ville, GA, USA) and Aerosol Spectrometer (GRIMM #1.108; GRIMM Inc.).

Working conditions including shift work, working hours and job stress were reviewed. Assessment of job stress, which was conducted in September 2007 by a local university, was evaluated in 445 workers in the departments where SCD cases were found, compared with 892 workers in other departments with no SCD cases. The assessment tool was the Korean Occupational Stress Scale which had been developed for Korean workers. It had eight subscales that included the physical environment, job demand, insufficient job control, interpersonal conflict, job insecurity, organizational system, lack of reward, and occupational climate [31].

Results

Overview of cases

All the SCD cases were male workers aged between 27 and 51 years when cardiac arrest happened (Table 1). The detailed diagnosis with ICD code for 5 cases, confirmed by autopsy, included one case of chronic IHD (I25), one case of IHD (I20-I25), two cases of acute myocardial infarction (I21), and one case of dilated cardiomyopathy (I42.0). Two cases for which autopsies could not be done were diagnosed as clinically suspected sudden cardiac death (I46.1). The deaths were distributed among the 4 seasons: spring (April and May), summer (July), autumn (September) and winter (November and December). Five cases (cases 1, 2, 3, 6 and 7) died at home or in a dormitory apartment after shift work or day work. Case 1 died while resting after morning shift work. Case 2 was found in a convulsive state at home during sleep after a night shift. Case 3 did a transplanting job for his parent's farming after a morning shift. Case 4 died in a dressing room of the company, while preparing his day shift which was to continue from the previous night shift. Case 5 died while waiting for dinner at a restaurant after the morning shift.

Work process

The tire manufacturing factory operated 2 manufacturing plants and one research institute, and employed 5,169 workers in 2007. Three cases were from manufacturing plant A, two cases from manufacturing plant B, and two cases from the research

Table 2. Chemical and physical agents of the sudden cardiac death (SCD) cases, December 2007

Case No.	Plant	Procedure	Job	CS_2 (ppm)	Styrene (ppm)	Rubber fume (mg/m^3) mean (interval)	Particulate matter particle number* (mean diameter†)	Noise (dBA) mean (interval)	Temperature (WBGT °C)
1	A	Curing	Production management: change of the bladder and mold	Trace-ND	ND	0.201 (0.086-0.334)	$3.74 \times 10^4 \pm 1.55$ (63)	83.2 (80.7-84.7)	18.9
3	A	Curing	Production management: change of the bladder and mold	Trace-ND	ND	0.201 (0.086-0.334)		83.2 (80.7-84.7)	18.9
2	A	Calendering	Setting of the mold	NA	ND	0.034 (0.031-0.037)	2.00×10^4 1.15 (75)	82.1 (75.5-86.3)	19.1
5	B	Calendering	Setting of the mold	NA	ND	0.275 (0.273-0.277)		82.9 (80.5-86.2)	19.1
4	B	All procedure	Facilities maintenance: troubleshooting of the facility	Trace-ND	ND	-	-	84.6 (80.5-89.3)	28.1

CS_2: carbon disulfide, ND: non-detected, NA: not available, WBGT: wet-bulb globe temperature, ppm: particle per million.
*Geometric mean (particles cm^{-3}) standard deviation, †geometric mean diameter in nanometer.

institute, plant C (Table 1). The process of tire manufacturing in the factory included compounding, banbury mixing, extruding, calendaring, bead building, tire building, and curing and finishing. In addition, there were two supporting departments: production management and facility maintenance. Production management managed the mold and bladder in the curing process. Facility maintenance addressed all problems with the machines, equipment, and other facilities of the factory. The SCD cases had been working in production management (cases 1 and 3), calendaring (cases 2 and 5), facility maintenance (case 4) and the research institute (cases 6 and 7). The detailed process of tire manufacturing in the factory is described in the investigation report [1].

Chemical and physical risk factors of the cases

Carbon disulfide and styrene were under the limit of quantitation. The concentration of carbon monoxide was under 1 ppm (Table 2). The highest concentrations of the other chemicals were 0.187 ppm for cyclopentane, 0.149 ppm for hexane, 0.010 ppm for n-hexane, 0.040 ppm for cyclohexane, 1.994 ppm for heptanes, 15.285 ppm for methylcyclohexane, 0.029 ppm for formaldehyde, and 0.083 ppm for sulfur dioxide. 1,3 butadiene was not detected.

The concentration of rubber fume in the SCD cases' department was 0.034-0.275 mg/m^3. The total PM assessed in October 2008 was 3.74 × 10^4 (± 1.55)/cm^3 in curing and 2.00 × 10^4 (± 1.15)/cm^3 in calendering (Table 2). It was 1.29 × 10^4 (± 1.51)/cm^3 in the outdoors, and 5.05 × 10^5 cm^3 around the diesel-powered forklift. The mean diameter of the rubber fume was 63 nm in curing and 72 nm in calendering (Table 2). The mean diameter of particulates was 12 nm in the diesel-powered forklift and 50 nm outdoors. Main PM sizes of the rubber fume in curing were distributed around 100 nm. PM sizes of diesel exhaust were distributed around 5 nm [30].

Forty-seven percent of workers were exposed to noise exceeding 85 dBA. The mean noise level of the SCD cases' department was 82-83 dBA. Mean heat exposure of the SCD cases department was 18-28 Wet-bulb globe temperature (WBGT) °C.

Non-Occupational factors and medical conditions of the cases

All cases were smokers or ex-smoker (Table 3). Except for cases 2 and 6, the others were drinkers. Case 6 was overweight, defined as body mass index (BMI) > 23. Cases 1, 2, 3 and 4 were obese, defined as 25 ≤ BMI. Three cases (1, 3 and 5) had hypertension (140 mmHg ≤ systolic pressure and 90 mmHg ≤ diastolic pressures); the other three cases (2, 4 and 6) had prehypertension (120 mmHg ≤ systolic pressure < 140 mmHg and 80 mmHg ≤ diastolic pressures < 90 mmHg). Case 2 had hypercholesterolemia with 252 mg/dL (reference ≤ 200 mg/dL). None of the cases showed high low-density lipoprotein (LDL) cholesterol (160 mg/dL ≤ LDL). High-density lipoprotein values for all cases were higher than the reference value, 40 mg/dL. Case 3 had high fasting blood sugar. Case 1 had an abnormal electrocardiography finding. None of the cases showed cardiac hypertrophy or proteinuria.

Shift work and job stress

Except for the cases from the research institute (cases 6 and 7), all cases had worked in shift work schedules including night shift for over 10 years in the factory (Table 4). The time table of cases 1, 2, 3, and 5 was three-shift of a four team schedule. Case 4 was on a two-shift schedule. The working time of the research institute was non-shifting (cases 6 and 7), from 09:00-to

Table 3. Chronic underlying medical conditions of the sudden cardiac death cases

Case No.	Smoking (pack/day)	Drinking	BMI	Blood pressure (mmHg)	Total cholesterol (mg/dL)	LDL/HDL (mg/dL)	Fasting blood sugar (mg/dL)	Electrocardiography
1	1-2	Yes	28.7	150/100	204	106.4/67	87	AF
2	0.5	No	26.4	135/85	252	145/55	98	NA
3	0.5-1	Yes	34.6	150/90	183	90.3/54.1	226	Normal
4	*	Yes	27.1	130/80	160	46.4/71	97	Normal
5	0.5-1	Yes	20.9	150/110	181	NA	91	Normal
6	Ex-smoker	No	24.7	120/70	195	113.1/58.7	77	NA
7	0.5-1	Yes	23.5	110/70	208	133/49	77	NA

BMI: body mass index (body weight in kg/ height in meter^2), LDL: low-density lipoprotein, HDL: high-density lipoprotein, AF: atrial fibrillation, NA: not available.
*Smoker but the amount is not available .

Table 4. Working hours and job stress of the seven the sudden cardiac death cases

Plant	Case No.	Date of hire	Working duration	Shift schedule at death	Working hours		Days of working holidays‡	Self description by their family or co-workers regarding the working environment
					One month*	One week†		
A	1	July '94	13 years	Morning shift (06:00-14:00)	185	48	16	Too hot (around 40°C), and dusty. Exhaustion especially in summer
A	2	January '95	12 years	Night shift (22:00-06:00)	199	61.5	22	Annoying by dealing the problematic machine
A	3	January '80	26 years	Afternoon shift (14:00-22:00)	160	40	8	-
B	4	October '92	14 years	First day of morning shift right after night shift	230	57	91	Burden of responsibility for maintenance of the machine which is the first step of the entire tire making process
B	5	July '95	11 years	Morning shift	189	40	33	Fatigue due to frequent overtime work
C	6	January '06	1 years	No shifting work	204	-	22	Stressful situation due to overtime work, and long working time until late night
C	7	January '06	1 years & 5 months	No shifting work	204	-	18	Stressful situation due to overtime work, and long working time until late night

*Average working hours per month of previous 1 year, †working hours of the previous week before death, ‡working holidays during previous 1 year.

18:00, with irregular variations. Average mean working hours per month during the previous one year was longest for case 4 (230 hours), while other cases had worked 160-204 hours per month. Working hours of the previous one week was more than 50 hours for case 2 (61.5 hours) and case 4 (57 hours). Case 4 had been working 16 hours continuously the day before he died; he had continued from a previous night shift to a morning shift on the same day. The complaints about their working conditions recorded by their family or co-workers was a hot environment (case 1), the burden of responsibility (case 4), and overtime work (cases 5, 6, and 7).

The results of job stress assessment showed that scores for physical environment, interpersonal conflict and the organizational system were higher in the departments where the SCD cases were found compared to control workers in manufacturing plant A. However, in manufacturing plant B, there was no significant difference. In the research institute (plant C), the score of insufficient job control was significantly higher than in control workers.

Discussion

Rubber fume has never been reported as a risk factor of CVD in the past, and has never been studied with regard to the size of the particles. Nanoparticles can be divided engineered or manufactured materials and non-intended materials. In the list of representative manufactured nanomaterials selected by the Working Party On Manufactured Nanomaterials of the Organization for Economic Cooperation and Development [32], rubber fume was not included. Major studies on non-intend materials were welding fume and combustion products of diesel exhaust. Therefore, the possibility of the existence of UFPs in rubber fume was unclear from previous studies. In our study, the mean diameter of rubber fume particles was 63 nm in curing and 72 nm in calendering (Table 2). There are no guidelines that define UFPs using the mean particle diameters, in case of non-intended, non-engineering materials, which are composed of various heterogeneous materials. However, the diameter of rubber fume in curing in our study was not larger than outdoor particles (50 nm). This result suggested that the particulate from rubber fume might be not significantly different from outdoor ambient particles.

Most epidemiological studies on cardiovascular effects were on the nanoscale fraction of environmental dusts rather than occupational exposure, although the mechanism is not fully understood [29]. In most of those studies, the effects are attributed to non-intended material combustion products [26], especially diesel exhaust [33]. In our study, the mean diameter

Table 5. Risk factors for cardiovascular diseases for the seven cases

	Occupational factors		Non-occupational factors
	Chemical & physical agents in the manufacturing process of the company	Characteristics of the job	
Acute	Chlorofluorocarbon (X)	Unexpected situations (outrage, surprise, excitement) related with work (X)	Unexpected situations (outrage, surprise, excitement) not related with work (X)
	Methylene chloride (X)	Physiologic disruption due to continuous long working hours (X)	Abnormality of electrolyte metabolism (X)
	High temperature (1,2,3,4,5)*	Maladjustment to abrupt change of the job (X)	Alcohol dinking (2,5)*
	Cold (X)		Drug (anti-arrhythmic drug, antidepressant) (X)
Acute or chronic	Organic nitrite (X)	Shift work (1,2,3,4,5)*	Hypertension (1,3,5)*
	Lead (X)	Long time work (2,4,5,6)*	Pre-hypertension (2,4,6)*
	Carbon monoxide (X)	Job stress (4,5,6)* Lack of exercise (X)	
Chronic	Arsenic (X)		Old age (more than 55 years old) (3)*
	Carbon disulfide (X)		Smoking (1,2,3,4,5,7)*
	Cobalt (X)		High blood lipid (2)*
	Fine particulate (1,2,3,4,5)*		Obesity (1,2,4)*, over weight (3,6,7)*
	Styrene aerosol (X)		Family history (not available)
	Noise (1,2,3,4,5)*		

X: do not exist or were not reported in individual records.
*Numbers in parentheses are case numbers.

of diesel exhaust was 12 nm, which was smaller than rubber fume particles. Considering this result, rubber fume has different characteristics compare to diesel exhaust, the most frequently studied UFP. Therefore, the strong relationship reported in previous epidemiological studies between particulate matter and CVD, cannot verify a causal relationship between rubber particulate and our SCD cases.

All chemical factors related to CVD such as carbon dioxide, carbon monoxide, and styrene that were reviewed in this study were found to be under the limit of detection (LOD) or were at a very low level (Table 2). The workers in this factory were not exposed to other chemicals related to cardiovascular risk such as chlorofluorocarbon, methylene chloride and cobalt. Thus, the possibility of chemical induced SCD was deemed to be low.

Among acute risk factors, high workplace temperatures and alcohol-containing drinks were found in our SCD cases (Table 5). No case had experienced unexpected outrage or surprise with or without work relatedness. No one had experienced physiologic disruption due to continuous long working hours. The high temperatures were found in all cases of manufacturing plants A and B (cases 1-5). Although the temperature measured in 2007 was lower than 30 WBGT °C (Table 2), it could not be evaluated precisely because this survey was done in December. The workers in the production management department who change molds in curing were exposed to 28.1 WBGT °C even when the outdoor atmosphere was 2.7 WBGT °C. The temperatures of curing and calendering were found to be more than 45 WBGT °C in summer [1], and the heat from these processes was spread to other processes. Therefore, except for cases 5 and 6, a high temperature could be a major acute triggering factor for SCD. Rogot and Padgett [21] reported an inverse, approximately linear pattern of CHD mortality with temperature over the greater part of the temperature range with average Fahrenheit temperatures in the 60's and 70's (15.6-26.6°C), and mortality rose sharply at higher temperatures. A Taiwan study also reported that the risk of coronary artery disease at 32°C was 22% higher than that at 26-29°C, especially in the elderly population [34]. Our SCD cases 1-5 could have been influenced by high temperature in the workplace, especially in the summer. However, only case 4 died in summer, whereas cases 2 and 3 died in the spring. Therefore, the causal relation-

ship between a hot environment and SCD were not clear.

Alcohol drinking was found in cases 2 and 5 (Table 5). Heavy drinkers (more than 6 drinks daily) are reported to have a significantly higher incidence rate of SCD than light drinkers (relative risk 2.00, 95% confidence interval 0.98 to 4.8) [35]. Case 2 had 1.5 drinks and case 5 had 6 drinks on the day of death. Therefore, alcohol consumption before death may have influenced the death of case 5.

Among risk factors which can influence health in an acute or chronic way, no chemical and physical factors were found in our SCD cases, but some occupational characteristics of the job and non-occupational medical conditions were found in some of these SCD cases (Table 5). Long hours of work are reported to increase the risk of CHD. More than 60 hours within a week or more than 11 hours per week over time work have been reported to increase acute myocardial infarction [36,37]. All the cases except 6 and 7 experienced shift work including night work. The mean working time per month during the previous 1 year for cases 1-5 was 185-230 hours, which was more than 160 hours (which is based on a working time of 8 hours per day, 5 days per week). Also, for the one week previous to death, the working time of cases 1 and 4 was higher than 40 hours and for case 2 was higher than 60 hours. In addition, these workers might have had an undesirable shift schedule, such as a night shift followed by a morning shift. For example the shift schedule of cases 4 changed from a night shift to a morning shift the day before he died, so that he had worked continuously for 16 hours. Therefore, cases 1, 2, 3, 4, and 5 had experienced shift work and an undesirable schedule. Although published evidence is suggestive but not conclusive for a relationship between shift work and CHD [20], all the SCD cases of manufacturing plant A and B had been working as shift workers for more than 10 years. Therefore, these workers can be influenced by overtime and shift work.

Cases 1-5 were exposed to noise exceeding 85 dBA for more than 10 years. One meta-analysis showed a significant association of occupational noise exposure and hypertension, with a relative risk per 5 dB(A) noise increase of 1.14 (1.01-1.29). However, the evidence for a relationship between noise exposure and IHD is still inconclusive because of the limitations in exposure characterization, adjustment for important confounders, and the occurrence of publication bias [17].

The blood cholesterol ratio, hypertension, cigarette smoking, excess weight, elevated blood sugar levels, lack of exercise, stress, and electrocardiographic abnormalities are well known risk factors of CHD [1]. All cases had at least two factors related to CHD. Six cases had hypertension or pre-hypertension, and were smokers. All cases except 5 were obese or overweight, and one of them had diabetes. One case had hyperlipidemia (Table 5). Thus, these risk factors must be part of the underlying cause of the SCD.

The possible etiologic or triggering occupational factors related to CVD in some of our 7 SCD cases were UFPs of rubber fume, hot environments, shift work in an undesirable schedule, and noise exposure. Among these factors, a dose-response relationship was reported only for overworking and a hot environment. Particulate characteristics of rubber fume were not clear. It was much larger than diesel exhaust, the most well known particulate, which has been found to have a causal relationship with CVD. The National Institute of Occupational Safety and Health in the US concluded that no conclusive data exist for a relationship between engineered nanoparticles or non-intended industrial particles generated in workplaces and workers' health. This appears to be due to a lack of comprehensive studies [38,39].

Considering that most of the cases had 1-3 non-occupational factors such as alcohol consumption, smoking, hypertension, overweight, underlying chronic health status was important to the SCD events, and it was influenced by shift work and high temperature. However, it will be necessary to continue studying the relationship between large sized UFPs and SCD.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Occupational Safety and Health Research Institute. Final report of epidemiological investigation on Hankooktire. Incheon (Korea): Occupational Safety and Health Research Institute; 2008. Report No.: 2009-22-434. Korean.
2. Nutt A. Rubber work and cancer--past, present and perspectives. Scand J Work Environ Health 1983;9(Suppl 2):49-57.
3. Fine LJ, Peters JM. Respiratory morbidity in rubber workers: I. Prevalence of respiratory symptoms and disease in curing workers. Arch Environ Health 1976;31:5-9.
4. Cleveland DE. Dermattis venenata in the rubber tire industry. Can Med Assoc J 1927;17:695-6.
5. Kromhout H, Swuste P, Boleij JS. Empirical modelling of chemical exposure in the rubber-manufacturing industry. Ann Occup Hyg 1994;38:3-22.
6. Lindbohm ML, Hemminki K, Kyyrönen P, Kilpikari I, Vainio H. Spontaneous abortions among rubber workers and congenital malformations in their offspring. Scand J Work Environ Health 1983;9(Suppl 2):85-90.

7. Special NIOSH hazard review: Rubber products manufacturing industry [Internet]. Cincinnati (OH): National Institute for Occupational Safety and Health. 2011 [cited 2011 Jul 12]. Available from: http://www.cdc.gov/niosh/docs/93-106/.
8. Peters JM, Monson RR, Burgess WA, Fine LJ. Occupational disease in the rubber industry. Environ Health Perspect 1976;17:31-4.
9. Oliver LC, Weber RP. Chest pain in rubber chemical workers exposed to carbon disulphide and methaemoglobin formers. Br J Ind Med 1984;41:296-304.
10. Tyroler HA, Andjelkovic D, Harris R, Lednar W, McMichael A, Symons M. Chronic diseases in the rubber industry. Environ Health Perspect 1976;17:13-20.
11. Delzell E, Sathiakumar N, Graff J, Matthews R. Styrene and ischemic heart disease mortality among synthetic rubber industry workers. J Occup Environ Med 2005;47:1235-43.
12. Wilcosky TC, Tyroler HA. Mortality from heart disease among workers exposed to solvents. J Occup Med 1983; 25:879-85.
13. Zipes DP, Wellens HJ. Sudden cardiac death. Circulation 1998;98:2334-51.
14. Forman SA, Helmkamp JC, Bone CM. Cardiac morbidity and mortality associated with occupational exposure to 1,2 propylene glycol dinitrate. J Occup Med 1987;29:445-50.
15. Hearne FT, Grose F, Pifer JW, Friedlander BR, Raleigh RL. Methylene chloride mortality study: dose-response characterization and animal model comparison. J Occup Med 1987;29:217-28.
16. Atkins EH, Baker EL. Exacerbation of coronary artery disease by occupational carbon monoxide exposure: a report to two fatalities and a review of the literature. Am J Ind Med 1985;7:73-9.
17. van Kempen EE, Kruize H, Boshuizen HC, Ameling CB, Staatsen BA, de Hollander AE. The association between noise exposure and blood pressure and ischemic heart disease: a meta-analysis. Environ Health Perspect 2002;110:307-17.
18. Theorell T, Karasek RA. Current issues relating to psychosocial job strain and cardiovascular disease research. J Occup Health Psychol 1996;1:9-26.
19. Knutsson A, Akerstedt T, Jonsson BG, Orth-Gomer K. Increased risk of ischaemic heart disease in shift workers. Lancet 1986;2:89-92.
20. Wang XS, Armstrong ME, Cairns BJ, Key TJ, Travis RC. Shift work and chronic disease: the epidemiological evidence. Occup Med (Lond) 2011;61:78-89.
21. Rogot E, Padgett SJ. Associations of coronary and stroke mortality with temperature and snowfall in selected areas of the United States, 1962-1966. Am J Epidemiol 1976;103:565-75.
22. Töro K, Bartholy J, Pongrácz R, Kis Z, Keller E, Dunay G. Evaluation of meteorological factors on sudden cardiovascular death. J Forensic Leg Med 2010;17:236-42.
23. Dal Grande M, Zanderigo C, Coato F, Menegolli S, Cipriani E, Pancheri V, Malesani F, Perbellini L. Sudden death caused by freon 22? Med Lav 1992;83:361-4.
24. Kaufman JD, Silverstein MA, Moure-Eraso R. Atrial fibrillation and sudden death related to occupational solvent exposure. Am J Ind Med 1994;25:731-5.
25. Schulz H, Harder V, Ibald-Mulli A, Khandoga A, Koenig W, Krombach F, Radykewicz R, Stampfl A, Thorand B, Peters A. Cardiovascular effects of fine and ultrafine particles. J Aerosol Med 2005;18:1-22.
26. Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A, Siscovick D, Smith SC Jr, Whitsel L, Kaufman JD; American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, and Council on Nutrition, Physical Activity and Metabolism. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation 2010;121:2331-78.
27. Rom WN. Environmental and occupational medicine. 4th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2007. 1931 p.
28. Cozzi E, Hazarika S, Stallings HW 3rd, Cascio WE, Devlin RB, Lust RM, Wingard CJ, Van Scott MR. Ultrafine particulate matter exposure augments ischemia-reperfusion injury in mice. Am J Physiol Heart Circ Physiol 2006;291:H894-903.
29. He F, Shaffer ML, Rodriguez-Colon S, Yanosky JD, Bixler E, Cascio WE, Liao D. Acute effects of fine particulate air pollution on cardiac arrhythmia: the APACR study. Environ Health Perspect 2011;119:927-32.
30. Occupational Safety and Health Research Institute. Epidemiological investigation on the environmental and health effect of tire manufacturing process. Incheon (Korea): Occupational Safety and Health Research Institute; 2009. Report No.: 2009-30-582. Korean.
31. Cho JJ, Kim JY, Chang SJ, Fiedler N, Koh SB, Crabtree BF, Kang DM, Kim YK, Choi YH. Occupational stress and depression in Korean employees. Int Arch Occup Environ Health 2008;82:47-57.
32. European Agency for Safety and Health at Work. Workplace exposure to nanoparticles. Bilbao (Spain): European Agency for Safety and Health at Work; 2009. 89 p.
33. Sydbom A, Blomberg A, Parnia S, Stenfors N, Sandström T, Dahlén SE. Health effects of diesel exhaust emissions. Eur Respir J 2001;17:733-46.
34. Pan WH, Li LA, Tsai MJ. Temperature extremes and mortality from coronary heart disease and cerebral infarction in elderly Chinese. Lancet 1995;345:353-5.
35. Wannamethee G, Shaper AG. Alcohol and sudden cardiac death. Br Heart J 1992;68:443-8.
36. Liu Y, Tanaka H; Fukuoka Heart Study Group. Overtime

work, insufficient sleep, and risk of non-fatal acute myocardial infarction in Japanese men. Occup Environ Med 2002;59:447-51.
37. Sokejima S, Kagamimori S. Working hours as a risk factor for acute myocardial infarction in Japan: case-control study. BMJ 1998;317:775-80.
38. Castelli WP. Epidemiology of coronary heart disease: the Framingham study. Am J Med 1984;76:4-12.
39. Nanotechnology. Frequently asked questions [Internet]. Atlanta (GA): Centers for Disease Control and Prevention. 2011 [cited 2011 Nov 3]. Available from: http://www.cdc.gov/niosh/topics/nanotech/faq.html